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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/016,869 | 01/30/1998 | DAVID H. BEACH | GPCI-P10-071 | 7533 |

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| EXAMINER |
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ROARK, JESSICA H

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| ART UNIT | PAPER NUMBER |
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1644

DATE MAILED: 06/27/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|------------------------------|------------------|--------------|--|
| Office Action Summary | Application N . | Applicant(s) | |
| | 09/016,869 | BEACH ET AL. | |
| | Examin r | Art Unit | |
| | Jessica H. Roark | 1644 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 March 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 91-95 and 98-112 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 91-93 and 103-105 is/are allowed.
- 6) ☒ Claim(s) 94,95,98-102 and 106-112 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 24 March 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input checked="" type="checkbox"/> Interview Summary (PTO-413) Paper No(s). <u>44</u> . |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____. | 6) <input type="checkbox"/> Other: _____. |

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RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 3/24/03 (Paper No. 42), is acknowledged.
Claims 96 and 97 have been cancelled. Claims 1-90 have been cancelled previously.
Claims 91-92, 94-95, 98, 103-104, 106, 108 and 111 have been amended.
Claims 91-95 and 98-112 are pending and under consideration in the instant application.
2. Applicant's Notice of Appeal, filed 3/24/03, is acknowledged. As per Applicant's directions in the Interview Summary of June 23, 2003, the Notice of Appeal is moot. The Period for Reply and Status of the Application is as indicated on the attached form PTO-326.
3. This Office Action will be in response to applicant's arguments, filed 3/24/03 (Paper No. 42),
The rejections of record can be found in the previous Office Action (Paper No. 39).

It is noted that New Grounds of Rejection are set forth herein.
4. Applicant's cancellation of claims 96 and 97 has obviated the previous objections and rejections with respect to these claims.

Drawings

5. The formal drawings filed 3/24/03 have been approved by the Draftsman.

Specification

6. Applicant's amendment, filed 3/24/03, has obviated the previous objection to the specification as failing to provide proper antecedent basis for the claimed subject.

Sequence Listing

7. After further review, it is noted that in the instant file, the amendment filed 2/28/02 (Paper No. 33) appears to be missing a portion of the Paper Copy of the Sequence Listing. The Paper Copy clearly indicates that there are 35 sequences in the sequence listing, and the CRF filed with the Paper Copy does contain 35 sequences.

Applicant is requested to provide:

- 1) an amendment providing a replacement copy of the Paper Copy of the Sequence Listing originally filed 2/28/02; and
- 2) a Statement that the replacement Paper Copy and the CRF originally filed 2/28/03 are identical.

A new CRF is NOT required.

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Claim Objections

8. Applicant's amendment, filed 3/24/03, has obviated the previous objection to claim 111.

9. It is noted for examination purposes that claims differing only by a recitation of an antibody that is "specifically reactive" versus an antibody that is "specifically *immunoreactive*" (e.g., claims 91 and 92) are considered to be restatements of the same subject matter and are not considered to differ in scope.

35 USC § 112 second paragraph

10. Applicant's amendment, filed 3/24/03, has obviated the previous rejection of claims 95-97 under 35 U.S.C. 112, second paragraph.

35 U.S.C. §§ 102 and 103

11. The Examiner acknowledges the amendment filed 3/24/03 amending the claims to delete reference to antibody "fragments" and "antibody preparations".

In view of the amendment filed 3/24/03, the instant claims appear to have adequate written support in priority document USSN 08/154,915 (11/18/93).

However, as was previously noted in Paper No. 36, the support with respect to various limitations appears to be as follows:

| | <u>'869 (instant)</u> | <u>'915 (11/18/93)</u> | <u>'997 (12/17/92)</u> |
|----------------------|-----------------------|------------------------|------------------------|
| p16 antibody kit | incorporated | page 28 | not found |
| labeled p16 antibody | incorporated | page 29 | not found |

In view of the apparent lack of adequate written support for kits and labeled p16 antibodies in USSN 07/991,997, instant claims 94-95, 98-102 and 106-112 do not appear to be entitled to an effective filing date of 12/17/92.

Applicant is invited to point to clear support for the above noted limitations of labeled antibodies and kits comprising in USSN 07/991,997.

35 U.S.C. § 102

12. In view of Applicant's amendment filed 3/24/03 and limiting the claims to subject matter that appears to have adequate written support in priority document USSN 08/154,915 (11/18/93), Kamb (U.S. Pat. No. 6,090,578, of record, earliest possible effective filing date 3/18/94) no longer appears to be available as a prior art reference against the instant claims.

Accordingly, the previous rejection of claims 91-95, 98-99, 101-110 and 112 under 35 U.S.C. 102(e) as being anticipated by Kamb has been obviated.

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13. In view of Applicant's amendment filed 3/24/03 and limiting the claims to subject matter that appears to have adequate written support in priority document USSN 08/154,915 (11/18/93), Skolnick et al. (US Pat No. 5,624,819, of record, earliest possible effective filing date 3/18/94) no longer appears to be available as a prior art reference against the instant claims.

Accordingly, the previous rejection of claims 91-95, 98-99, 101-110 and 112 under 35 U.S.C. 102(e) as being anticipated by Skolnick et al. has been obviated.

Claim Rejections – 35 U.S.C. § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

15. Claims 94-95, 98-102 and 106-112 are rejected under 35 U.S.C. 103(a) as being unpatentable over Xiong et al. (Genes & Dev. August 1993; 7:1572-1583, IDS #EO) in view of Busch et al. (US Pat No. 4,794,077, of record).

Applicant's arguments, filed 3/24/03, have been fully considered but have not been found convincing.

Applicant argues that in view of the amendment filed 3/24/03 the instant claims are supported in the '997 priority document and the Xiong et al. reference is antedated.

However, although certain limitations are support in the '997 application as acknowledged supra; the instant claims still contain limitations which do not appear to have adequate written support in the '997 application.

Consequently, the Xiong et al. reference published in August 1993 is available as prior art under 35 USC 102(a) with respect to these pending claims.

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It is again noted that the Beach Declaration under 37 CFR 1.132 filed 9/9/02 is insufficient to overcome the rejection of the instant claims based upon the Xiong et al. publication because co-inventors Demetrick, Serrano and Hannon are not co-authors on the Xiong et al. publication. Thus the printed publication is still by "another" and available as prior art under 35 USC 102(a).

It is also noted that the rejection of record (re-iterated below) relies upon the teaching of the p16 protein as the basis for the rejection, rather than the antibody addressed in the Beach Declaration.

Although a reference that is not a statutory bar under 35 USC 102(b) may be antedated, in order to antedate a reference a proper Declaration under 37 CFR 1.131 (or 37 CFR 1.132, if appropriate) must be filed (MPEP 7.15.01(d)).

Therefore, Xiong et al. still appears to be available as a reference under 35 USC 102(a) with respect to the above noted claims.

The rejection of record in Paper Nos. 36 and 39 is reiterated below as applied to the instantly pending claims:

The claims are drawn to antibodies conjugated to a detectable label and kits comprising antibodies wherein the antibodies bind a 16 kD protein that coprecipitates with CDK4 from lysate of SV40-transformed WI38 cells in the presence of an anti-CDK4 antibody (which is the same as a protein comprising SEQ ID NO:35).

Xiong et al. teach a p16 cell cycle regulatory protein that is 16 kD and that binds to and coprecipitates with the cyclin-dependent kinase CDK4 from cell lysate of SV40-transformed WI38 cells in the presence of an anti-CDK4 antibody (see entire document, especially Figure 1). Xiong et al. teach that the molecular identity of p16 was unknown, but that it associates with proteins involved in cell cycle progression that are altered in oncogenically transformed cells, and that studies addressing possible altered responses involving cell cycle regulatory proteins are important to understanding oncogenesis (e.g., see "Discussion"). Xiong et al. purify p16 from several human cellular sources, including the WI38 cell line transformed with SV40 (the VA13 cell line, see "Cell Culture" on page 1581) and provide a peptide map to show that p16 is the same in each case (e.g., Figure 6). Xiong et al. also teach the production of antibodies to other proteins involved in cell cycle regulation (see entire document, especially "Antibodies and Immunological Methods" on page 1581), and use these antibodies to study the association and expression of various cell cycle proteins (see entire document).

Xiong et al. do not teach antibodies conjugated to a detectable label and kits comprising antibodies an antibody to a 16 kD protein that coprecipitates with CDK4 from lysate of SV40-transformed WI38 cells in the presence of an anti-CDK4 antibody, nor an antibody to p16.

Busch et al. teach and claim a kit comprising an antibody to a cell cycle regulatory protein (p145) and a detectable label for detecting the antibody (see entire document, especially claims 3-15 and column 11). Means for detecting the cell cycle regulatory protein are taught that include both a detectable label conjugated to the antibody (e.g. column 11 at lines 15-26 and claim 16) and a second antibody (e.g., column 11 at lines 27-41). Both monoclonal and purified polyclonal antibody preparations are taught (see entire document, especially claims 3-5 and 14-15). Busch et al. teach throughout the reference that the antibodies are formulated for detecting the protein in samples of cells (e.g., columns 7-8).

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Given the teachings of the references, it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare antibodies to the p16 taught by Xiong et al. and to provide those antibodies conjugated to a detectable label and in kit form. Given the teachings of Xiong et al. that p16 is associated with CDK4 and involved in cell cycle progression and possibly the mechanism underlying oncogenesis, one of ordinary skill in the art would have been motivated to provide an antibody to p16, including a labeled antibody or kit comprising, in order to study p16's role in cell cycle and oncogenesis. As taught by both Xiong et al. and Busch et al., one of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of successfully producing antibodies to p16 and formulating them in various diagnostic kits for detecting p16 in a sample of cells. Although the amino acid sequence of p16 is not taught by either reference, the sequence is an intrinsic property of the protein and thus a recitation of sequence composition does not render an antibody to the protein unobvious. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

16. In view of Applicant's amendment filed 3/24/03 and limiting the claims to subject matter that appears to have adequate written support in priority document USSN 08/154,915 (11/18/93), neither Kamb (U.S. Pat. No. 6,090,578, of record, earliest possible effective filing date 3/18/94) nor Skolnick et al. (US Pat No. 5,624,819, of record, earliest possible effective filing date 3/18/94) appears to be available as a prior art reference against the instant claims.

Accordingly, the previous rejection of claims 96-97 under 35 U.S.C. 103(a) as being unpatentable over either Kamb or Skolnick et al. in view of Owens et al. (J. Immunol. Methods February 1994; 168:149-165, of record) has been obviated.

Conclusion

17. Claims 91-93 and 103-105 appear to be allowable. However, the indicated allowability of claims 91-93 and 103-105 is subject to further review pending a determination of a possible interference.

18. Applicant's amendment necessitated the new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

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19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jessica Roark, whose telephone number is (703) 605-1209. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Jessica Roark, Ph.D.
Patent Examiner
Technology Center 1600
June 26, 2003

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